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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
08/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,203	COSENZA, LAWRENCE W.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-42* is/are pending in the application.

4a) Of the above claim(s) *3,10,12,14-40 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-9,11,13 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Applicant's amendment and response received on 6/6/07 has been entered. Claim 5 has been canceled. Claims 1-4, and 6-42 are pending in the instant application. This application contains claims 3, 10, 12, 14-40, and 42 drawn to an invention nonelected without traverse, there being no allowable generic or linking claim. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-2, 4, 6-9, 11, 13, and 41 are currently under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Drawings

Applicant's submission of a substitute Figure 9 in the 3/6/07 response is acknowledged. The new drawing is legible and in compliance with 37 CFR 1.121(d). The objection to the drawing is withdrawn.

Nucleotide and Amino Acid Sequences

Applicant's amendment to the specification submitted with the 3/6/07 response inserted SEQ ID NOS in paragraphs starting on pages 6, 11, and 29 is acknowledged. However, page 29

continues to recite two amino acid sequences which are not identified by SEQ ID NOS. The sequences "MGAQ" and "MAIS" on page 29 meet the definition of amino acid sequences set forth in 37 CFR 1.821 which states that amino acid sequences of four or more amino acids must be identified by SEQ ID NOS, see 37 CFR 1.821(a) and (d). Therefore, this application continues to fail to comply with the requirements of 37 CFR 1.821 through 1.825. Full compliance with the sequence rules is required in response to this Office Action.

A complete response to this office action should include both compliance with the sequence rules and a response to the rejections set forth in this office action. Failure to comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Specification

The objection to the disclosure because of informalities on page 3 is withdrawn in view of the amendment to page 3 in the 3/6/07 response.

35 U.S.C. 132

The amendment filed 3/6/07 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: on page 29, the applicant has amended the specification to delete "(CCT GGT) to (CCG GGG)"(Pro Gly)" from the sentence that originally read, "The

silent mutations alter the native nucleic acid sequence (CCT GGT) to (CCG GGG) but will not change the protein composition (Pro Gly). Deletion of the nucleotides and amino acids from this sentence constitutes new matter since it substantially changes the breadth of the teachings regarding the introduction of silent mutations. The original specification teaches that a specific mutation caused by the introduction of an Avr I restriction site which is (CCT GGT) to (CCG GGG). This portion of the specification as amended now teaches the introduction of an Avr I restriction site anywhere in the VP4s as long as the introduction doesn't change the protein composition and thus significantly broadens the teachings of the specification beyond what was originally disclosed. As such, the amendment to this section introduces new matter to the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The rejection of claims 1-2, 4-9, 11, 13, and 41 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn over canceled claim 5 and maintained over amended claims 1-2, 4, 6-9, 11, 13, and 41. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that the claims have been amended to recite a primate Hpr and that Lugli et al. shows Hpr is only found in primates and that only humans, baboons and chimpanzees posses full length Hpr. The applicant further argues that these three sequences have high homology and that since there are only three members of the genus, the sequences described in

the specification is representative of the genus. In response, it is noted that the Lugli et al. reference was not provided for consideration by the examiner and is not of record in the instant application. In addition, Lugli et al. was published in 2004 several years after the effective filing date of the instant application. Thus, Lugli et al. does not represent what was known in the prior art at the time of filing. The applicant is reminded that compliance with 35 U.S.C. 112, first paragraph, for written description is determined based on the disclosure in the specification in view of the state of the art at the time of filing. See MPEP 706.03 and form paragraph 7.31.01 which was set forth in the previous office action and which states; "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (emphasis added by examiner). The rejection of record discussed the disclosure in the specification in view of the state of the prior art and concluded that the specification does not provide sufficient written description for the genus of Hpr proteins or nucleic acids encoding Hpr proteins other than human Hpr protein and a cDNA encoding human Hpr. The rejection of record discussed that the specification provides guidance for cloning the nucleic acid encoding human Hpr from the human hepatic carcinoma cell line HepG2. However, aside from the human Hpr nucleic acid sequence and encoded amino acid sequence, the specification does not provide any additional description for any other Hpr genes or proteins from any other species of animal including the genus of primates. Further, Smith et al. teaches that serum lytic activity is only observed in some apes and Old World monkeys and that in non-human primates the only known Hpr gene is found in Chimpanzees, where the gene does not express functional protein due to premature termination of translation (Smith et al.

(1995) Science, Vol. 268, 284-286, see pages 285-286, bridging paragraph). Thus, neither the specification or the prior art provides an adequate description for any Hpr gene or protein other than human Hpr. While applicant argues that the teaching of Lugli et al. establish that there are three species of primates that express the full length Hpr gene, this does not reflect the knowledge of the skilled artisan at the time of filing and does not show that the applicant was in possession of the genus of primate Hpr as of 2002 , the effective filing date. Thus, the rejection for lack of written description for the genus of primate Hpr is maintained.

In regards to the lack of written description for the genus of genes encoding a small interfering RNA related to a therapeutic agent, where the therapeutic agent is a drug or prodrug, the applicant argues that the elected invention of a organism containing a drug or prodrug encompasses siRNA or miRNA. The applicant states that the specification broadly defines drugs and prodrugs to fully encompass siRNA and miRNA and that the specification references a number of publications that teach siRNAs useful in the invention as claimed. In response, the original claims which recited, "a sacromastigophoric organism containing said therapeutic agent" was identified as a linking claim in the restriction requirement which identified several independent and distinct inventions linked by the use of the term "therapeutic agent". These independent inventions encompassed by "therapeutic agent" included genes, artificial chromosomes, magnetic species, radioactive species, vitamins, nanocrystals, and drugs or prodrugs. In response to this restriction requirement, the applicant elected without traverse the invention drawn to an organism containing a drug or prodrug. While the specification broadly defines a "therapeutic agent" to include various substances capable of treating a disease, it is not agreed that the specification broadly defines a drug or prodrug to encompass the same breadth of

compounds as encompassed by a "therapeutic agent". The rejection of record pointed specifically to page 11 of the specification for the definition of drug/prodrug. This entire paragraph is set forth below for clarity:

The term "drug" is defined as compounds used as a medicine to treat a disease, disease system, or undiagnosed pain. Drugs, as used herein, are typically small organic molecules having a molecular weight of less than 1000 and illustratively include channel blockers, receptor blockers, steroids, opioids, platinum compounds, terpenoids, and alkaloids. As used herein, drugs include pharmaceutically acceptable salts, esters, and amides of active medicinal species.

The term "prodrug" is defined as compounds that are rapidly transformed in vivo to yield the parent compounds of the above formula, for example, by hydrolysis in blood. (T. Higuchi et al. 1987). (emphasis added)

Thus, contrary to applicant's arguments, drugs are taught in the specification to be small organic molecules having a molecular weight of less than 1000 and include channel blockers, receptor blockers, steroids, opioids, platinum compounds, perenoids and alkaloids. Further, page 8 of the specification clearly teaches that "gene" as used in the specification includes siRNA and miRNA. The applicant did not elect a "gene" as the therapeutic agent. As such, applicant's arguments regarding siRNA or miRNA as the therapeutic agent are not on point as a "gene" is not the elected subject matter.

In addition, the rejection of record was based on the lack of written description for the further inclusion of a gene encoding an siRNA "related" to said therapeutic agent which is a drug or prodrug. This limitation is present in claim 9. The rejection of record stated that while page 9 of the specification provides a general definition of small interfering RNA, the specification provides no further guidance as to any specific genus or species of siRNA, much less siRNA related to a drug or prodrug. The specification further fails to provide any specific

guidance as to the structural, chemical, or physical properties of siRNA "related" to a drug, such that methods for identifying or isolating any such siRNA could be determined. In the absence of any such information, the skilled artisan cannot envision the detailed chemical structure of any siRNA species related to a drug or prodrug as claimed. Regarding claim 9, the applicant argues that HGPRT was known in the art as an improved therapeutic agent for converting the cancer prodrug allopurinol, citing Trudeau et al., and that siRNA related to cancer therapy are well known in the art citing Yin et al., Butz et al., Chen et al. and Howard et al. In response, it is first noted that none of the cited references with the exception of Trudeau et al. are of record or have been provided to the examiner for consideration. However, while it is agreed that various drugs and prodrugs were known in the prior art, all of the cited references purportedly teaching siRNA were published after the effective filing date of the instant application. Thus, Yin et al., Butz et al., Chen et al. and Howard et al. cannot be relied upon as evidence of what was known in the prior art at the time of filing. Therefore, it is maintained that the applicant has not provided any description or reduction to practice of siRNA related to a drug or prodrug, including HGPRT or allopurinol. Based on the applicant's specification, the skilled artisan cannot envision the detailed chemical structure of the genus of siRNA encompassed by the claims. Therefore, the rejection of record is maintained.

The rejection of claims 1-2, 4-9, 11, 13, and 41 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn over canceled claim 5 and maintained over amended claims 1-2, 4, 6-9, 11, 13, and 41. Applicant's amendments and

arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

Applicant's amendments to the claims to clearly recite that the organism comprises a gene encoding primate Hpr overcomes the grounds of rejection based on making and using a Trypanosome by introducing a Hpr protein into the organism. The amendments also overcome previous grounds of rejection based on the lack of a lysosomal targeting sequence and the breadth of the promoter sequence. However, the amendments to the claim do not overcome the lack of enablement for making any Trypanosome which contains a recombinant nucleic acid encoding a Hpr and which additionally contains a drug or prodrug or using any such organism as a therapeutic delivery system.

The applicant argues that the specification provides concrete examples which enable the invention as claimed including the construct taught in Figure 1 which includes a gene encoding Hpr operably linked to a Tet inducible promoter, and example 3 which teaches that the recombinant Hpr gene contains a lysosomal targeting sequence. The applicant also argues that genetic transformation of single cell organisms is well known in the art and that the specification teaches that Hpr localized to the lysosome lyses Trypanosomes. In response, the teachings of the specification, including the working examples, were analyzed and discussed in detail in the previous office action and were not found sufficient to enable the instant invention. In particular, the rejection of record discussed that while the specification teaches the construction of an inducible expression construct comprising the cDNA for human Hpr operatively linked to a p67 lysosomal targeting sequence and further operatively linked to an tetracycline inducible T7 promoter, as shown in Figure 9, and the construction of a modified retroviral transposon to be

delivered using a Trypanosome, the elected invention is drawn to the delivery of a drug or prodrug, not a virus, as the therapeutic agent. While the working examples teach the construction of an expression vector as shown in Figure 9 and described above, the examples do not include any data from any actual experiments demonstrating infection of any type of host cell followed by lysis of the host cell mediated by Hpr. Examples 5 and 6 appear to be prophetic examples describing experiments to test the ability of Trypanosomes containing an expression vector to mediate gene transfer in human or mice cells *in vitro* or *in vivo*. These prophetic examples do not demonstrate actual lysis of Trypanosome infected cells through expression of Hpr, nor do they demonstrate or suggest the delivery of any drug or prodrug using the Trypanosome. Regarding applicant's arguments that working examples are not required to establish enablement and that prophetic examples can be sufficient to satisfy the enablement requirement, the applicant agrees that working examples are not required if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). However, lack of a working example is a factor to be considered, especially in a case involving an unpredictable and undeveloped art (MPEP 2164.02). In the instant case, the rejection of record is not based on the lack of working examples which demonstrate lysis of any Trypanosome by inducing the expression of a gene encoding Hpr operatively linked to a lysosomal targeting sequence, the previous office action analyzed the specification in direct accordance to the factors outlined in *In re Wands*, namely 1) the nature of the invention, 2) the state of the prior art, 3) the predictability of the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of the skilled artisan,

and 8) the breadth of the claims, and presented detailed scientific reasons for the finding of a lack of enablement for invention as claimed. It is also noted that case law including the Marzocchi decision sanctions both the use of sound scientific reasoning and printed publications to support a holding of non-enablement (see *In re Marzocchi* 169 USPQ 367, and *Ex parte Sudilovsky* 21 USPQ2d 1702). Further, the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). 35 U.S.C. 112 also requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

Further, despite applicant's argument that the specification states that delivery of Hpr to the lysosome will result in lysis of Trypanosomes, the rejection of record included evidence that not all species of Trypanosoma appear to be susceptible to Hpr mediated lysis, citing Shimamura et al. Regarding Shimamura, the applicant further argues that the failure of Hpr to lyse the subspecies *Trypanosoma brucei rhodensiense* was the result of inadequate endocytosis and lysosomal targeting and that since the claims now recite that the Hpr gene includes a lysosomal targeting sequence that the Hpr protein will be localized to the lysosome thus bypassing endocytosis and leading to lysis of *Trypanosoma brucei rhodensiense* as well as *Trypanosoma brucei brucei*. In response, this not agreed as Shimamura et al., while suggesting that the lack of lysis of *Trypanosoma brucei rhodensiense* may be due to reduced endocytosis and failure to enter the lysosome, does not teach that the exact reason for the failure of TLF-1 containing Hpr to lyses *Trypanosoma brucei rhodensiense* had been determined. Neither Shimamura et al. nor

the instant specification demonstrates that improving intracellular targeting of Hpr to the lysosome would in fact result in lysis of *Trypanosoma brucei rhodensiense*. Thus, applicant's argument does not overcome the lack of enabling disclosure for lysing any Trypanosome, including any subspecies of *Trypanosoma brucei*, by introducing a gene encoding Hpr and a lysosomal targeting sequence.

The applicant also reiterates their arguments from the written description rejection concerning the use of primate Hpr genes and the use of various genes as the drug in the elected invention. These arguments were addressed in detail in the response to applicant's arguments regarding lack of written description above. In short, it is maintained that the elected invention is not "genes" and that the specification does not define drug or prodrug to encompass genes. The applicant is again referred to the restriction requirement which set forth the independence and distinctness of the different inventions and their own election without traverse of the invention where the therapeutic agent is a drug or prodrug, not a gene. Also, as noted above, applicant's evidence for description of species of Hpr other than human Hpr is post-filing and does not represent the state of the art as of the effective filing date of this application.

Finally, the applicant argues that methods for fusing liposomes with eukaryotic cells was well known in the art such that the teachings of the specification for creating liposomally packaged therapeutic agents combined with the teachings in the art sufficiently enables the delivery of a drug or prodrug using the claimed methods. In response, the rejection of record states that the only guidance relevant to drug delivery provided by the specification occurs on page 18, which states that, "Non-nucleic acid therapeutic agents are packaged in a sacromastigophoric organism through electroporation or phagocytosis of liposomally packaged

therapeutic agents" (specification, page 18, lines 8-10). It is noted, however, that the claims are not limited to Trypanosomes containing liposomally packaged drugs or prodrugs. The specification then points to US Patents 4,356,167, 4,873,088, and 5,843,475 are providing guidance for liposomal packaging processes. However, these patents, while teaching methods to make liposomes containing various chemical compounds or drugs, does not provide any guidance for actually introducing the liposomes into a Trypanosome or further teach the fate of such liposomes once in the Trypanosome. Neither the specification nor the prior art of record teaches that drugs, either packaged in a liposome as described by any of the reference patents or not, can be stably maintained in a Trypanosome, or subsequently released to a host organism upon lysis of the Trypanosome. Further, while the specification on page 18 goes on to teach that the organism containing a non-nucleic acid therapeutic must be administered in a therapeutic amount, the specification fails to teach how much or any type of drug can be contained within a single Trypanosome or what amount of drug containing Trypanosome must be delivered to release a therapeutic amount of the drug to a host. Further, regarding the applicant's citation of Anzar et al., Mizoue et al., Kunisawa et al. and Nakanishi et al. as evidence regarding the fusion of liposomes and eukaryotic cells, none of the references are of record or have been provided to the examiner for consideration. As such, the relative merits of the teachings of any of these references to the enablement of the instant invention as claimed cannot be determined.

Thus, in view of the state of the art, which does not teach the inclusion of drugs or prodrugs in Trypanosomes or the use of such Trypanosomes to deliver therapeutic amounts of drugs to a host, the lack of any specific guidance for modifying a Trypanosome to contain any

amount of any drug or prodrug, the lack of working examples, and the breadth of the claims, it would have required undue experimentation to make and use the Trypanosomes as claimed.

The rejection of claims 1, 7-8, 11, 13 and 41 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn over claims 1, 11, 13, and 41 in view of applicant's amendments to the claims and maintained over claims 7-8. The applicant argues that the amendments have overcome the grounds for rejection. However, claim 7 continues to recite that the recombinant lytic factor is upregulated by a promoter, which is confusing as it is unclear how a protein can be "upregulated" by a promoter.

Applicant's amendments have necessitated the following new grounds of rejection under 35 U.S.C. 112, second paragraph as set forth below.

Claims 7-8 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 depends on claim 1 and recites the limitation "said recombinant lytic factor". However, as claim 1 has been amended to delete the phrase " recombinant lytic factor", there is insufficient antecedent basis for this limitation in the claim. In addition, it is noted that claim 1 has been amended to include the limitation of an inducible promoter, as such, it is unclear whether the promoter referred to in claim 7 is the same promoter referred to in claim 1. Claim 8 depends on claim 7 and thus is included in this rejection.

Claim 41 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 41 recites the limitation "said primate Hpr protein" in line 8; however, there is insufficient antecedent basis for this limitation in the claim. Note that in line 7, the claim recites, "primate Hpr". Amendment of this to "primate Hpr protein" would overcome this rejection.

Claim 1 recites a therapeutic delivery system comprising a therapeutic agent and sacromastigophoric organism containing said therapeutic agent and a recombinant lytic factor. Claim 7, which depends on claim 1, further recites, "wherein said recombinant lytic factor is upregulated by a promoter responsive to an induction species exogenous to both said organism and said host". A "recombinant lytic factor", as recited in claim 1, is a protein, not a gene encoding a recombinant lytic factor. As such, claim 7 is confusing as it is unclear how a recombinant protein can be "upregulated" by a promoter since promoters drive expression of genes and thus can only upregulate the "expression" of a protein. Claim 11 recites that same language as claim 8. Claims 8 and 13 depend on claims 7 and 11 respectively and thus have been included in this rejection.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633

Application No.: 10/735,203

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. Other: sequences on page 29 are not identified by SEQ ID NOS

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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